

IIV brainstorm
COVID-19 clinical vaccine trials

Dec 2nd 2020

Agenda for *this* meeting:

- 11.00: Introduction of context
- 11.05: Overview of provided input
- 11.15: Discussion
- 11.50: Summary of primary questions
- 12.00: End

Later:

Keeping you all informed

Research context:

- IIV: Public Health
- Cib / RIVM
- Academia
- Pharma
- Consortia
- (MoH)

assessment of research context is ongoing

Our primary question:

Which are, from a Public Health perspective, the clinical vaccine trial(s) the RIVM/IIV should perform?

In other words, how can we assess vaccine-induced protection against COVID in the Dutch population?

Our secondary question:

Which are the immunological questions therefore to be addressed in such a trial?

Visional, not operational

General

1. Primary: which are clinical vaccine trials the IIV could perform?	2. Secondary: immunological questions to be addressed in trial?	3. Mechanism / how (examples)?	Input by...
Do vaccines protect the Dutch population... ? - from disease - from severe disease - from infection	A. Which are vaccine-induced correlates of protection? - Innate, T cell / B cell (incl. memory), antibody levels, avidity, functionality, neutralization, glycosylation, etc etc - B. How does vaccination compare to natural infection? C. Which are microbiome correlates for vaccine take?	How do these responses protect? - Neutralization - Fc functionality - Cytotoxicity, ADCC etc etc How does microbiome modulate vaccine responses (and can we modulate the modulators)?	5.1.2e
Do vaccines protect against transmission?	A. Which are vaccine-induced CoP from transmission? B. How does vaccination protect against transmission, compared to natural infection?		5.1.2e
How long does vaccine-induced protection last.....? - in the population - in subgroups, eg. the elderly	Which are vaccine-induced correlates of protection and how long do these responses last?	Immune senescence etc.	5.1.2e
How do vaccines compare in immune protection?	A. How do vaccines compare in CoP (from disease, transmission)? B. How do vaccines compare in longevity of responses? C. How do vaccines compare in age groups / the elderly?	How is vaccine design / vaccine platform linked to immunity?	5.1.2e
Can different vaccines be used for primary and booster doses; and then which intervals should be applied?			5.1.2e
Are there disadvantageous immune consequences of vaccination? What is the impact of preexisting immunity to CoV2 or other coronaviruses on vaccination?	Which are risks of infection-induced hyperinflammation following vaccination? Which are risks of vaccine-induced hyperinflammation following preexisting immunity (CoV2 or seasonal)?	- ADE - Antigenic sin - Crossreactive T-cells	5.1.2e

Subgroups

1. Primary: which are clinical vaccine trials the IIV could perform?	2. Secondary: immunological questions to be addressed in trial?	3. Mechanism / how (examples)?	Input by...
Are the elderly protected by novel, emerging vaccine platforms? Check input annemarie	A. How do vaccine platforms compare in an aging population (eg. mRNA vs. vector vs. conventional/subunit)? B. Do CoP differ between young and elderly? C. Does longevity of responses differ between young and elderly? A. Is immunity linked to age, frailty Index / comorbidities?	Fc functionality compared between platforms in the elderly How are comorbidities, age and inflammation interrelated within vaccine-induced immunity?	5.1.2e
Are the obese protected by novel, emerging vaccine platforms?	iter	iter Hyperinflammation related to obesity	5.1.2e
Clinical subgroups covered by national consortia: <ul style="list-style-type: none"> • Immunocompromised: autoimmune, immune therapy > Target2B • Cancer patients > VOICE consortium Other clinical subgroups, need to check with 5.1.2e / LCI: <ul style="list-style-type: none"> • Chronic respiratory diseases • Chronic heart disease • Diabetes mellitus • Chronic kidney disease • Transplant patients 	A. Is immunogenicity different in these patients compared to controls and is there a difference in CoP? A. Which are microbiome correlates for vaccine take?	Immune senescence Microbiome modulation	5.1.2e
Do vaccines protect pregnant women and their newborn from infection/disease, including in utero and perinatal infection? Is it safe to vaccinate pregnant women?	A. Is immunogenicity different in pregnant women compared to controls and is there a difference in CoP in pregnancy? B. Does vaccination lead to antibody transfer in utero / can antibodies be detected in cord blood?	Mechanisms of maternal immunity, antigen presentation, NK cell function etc.	5.1.2e